Updates to USP 797/USP 800

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Disclosure

The presenter has no conflicts of interest to disclose
Objectives

1. Review highlights of USP <797> and <800> as currently published.
2. Discuss current compliance trends in sterile compounding in accordance with USP guidelines.
3. Describe the most significant upcoming changes to USP <797>.
4. Explain the impact of USP updates on current sterile compounding practices.
Currently USP Chapter 797 addresses sterile compounding of non-hazardous and hazardous preparations.

A. TRUE

B. FALSE
Pre-test Question 2

USP Chapter 800 is already in effect.

A. TRUE
B. FALSE
What is the role of USP in pharmacy and medication management?

A. USP inspects pharmacies
B. USP provides guidelines and standards
C. USP regulates compounding
D. USP enforces its regulations
Pre-test Question 4

USP Chapter 800 requires all of the following engineering controls to be in place for Containment Segregated Area except:

A. Minimum of 12 air exchanges per hour
B. Negative pressure gradient to anteroom
C. Appropriate primary engineering controls
D. Terminally HEPA filtered air to achieve ISO 7
Sterile Compounding Regulatory Hierarchy

- FDA
- State Board of Pharmacy
- USP 797 and 800
- NIOSH
- ASHP Best Practices
- Industry Guidance Documents
Current Regulatory Environment

Overview

- USP Chapter 797 currently in effect, but under revision
- Since July 2014 FDA issued more than half a dozen of regulatory documents that impact pharmacy practice and compounding (on FDA website Compounding tab)
- FDA has been auditing facilities (including hospitals and compounding pharmacies)
USP Chapter 797 Scope Review

• To provide guidelines to prevent harm, including death, to patient (human or veterinary) that may be caused by:
  – contamination
  – improper compounding technique

• Considered minimum practices and standards

• Control of compounding personnel, environment and processes
Chapter 797 Overview

• List of responsibilities of compounding personnel
• Definition of CSP microbial contamination risk levels
• Requirements for personnel training and evaluation of aseptic manipulation skills
• Guidelines on verification of compounding accuracy and sterility
• Basics of environmental QC
Chapter 797 Overview

- Gowning guidelines
- Hazardous sterile compounding guidelines
- Suggested SOPs
- Elements of QC, QA, final checks and tests
- BUDs, stability and storage recommendations
- Guidelines on maintenance of sterility, purity, and stability of CSPs
# BUD versus Expiration Date

<table>
<thead>
<tr>
<th>EXPIRATION DATE</th>
<th>BEYOND-USE DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Assigned by the manufacturer</td>
<td>• Assigned by a pharmacist</td>
</tr>
<tr>
<td>• Determined using stability studies</td>
<td>• Determined based on current scientific literature</td>
</tr>
<tr>
<td>designed based on FDA guidelines</td>
<td>or per manufacturer recommendations</td>
</tr>
<tr>
<td></td>
<td>• USP reference</td>
</tr>
</tbody>
</table>
## Definition of CSP Microbial Contamination Risk Levels

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Description</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low Risk</strong></td>
<td>Mixing of no more than three sterile products and no more than two separate entries into the sterile container, prepared in ISO5 or better</td>
<td>Reconstitution of one vial of drug to one minibag, transferring contents of ampule to a container</td>
</tr>
<tr>
<td><strong>Medium Risk</strong></td>
<td>More complex than low risk, multiple injections of several products, prepared in ISO5</td>
<td>TPN preparation, batch compounding</td>
</tr>
<tr>
<td><strong>High Risk</strong></td>
<td>Use of one or more products that are not sterile and will be sterilized in the process prior to use, not in ISO5, improper gowning</td>
<td>PCA prepared from a powdered drug in bulk</td>
</tr>
<tr>
<td><strong>Immediate Use</strong></td>
<td>Prepared in emergency for immediate patient administration, may include diagnostic products, must administer within 1 hour of preparation</td>
<td>Life-saving drug prepared for a patient in ER</td>
</tr>
</tbody>
</table>
Beyond Use Dating per USP<797>

<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Stored at room temperature (20-25°C)</th>
<th>Stored under refrigeration (2 to 8°C)</th>
<th>Stored in freezer (-10 to -25°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Use</td>
<td>1 hour</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Low Risk</td>
<td>48 hours</td>
<td>14 days</td>
<td>45 days</td>
</tr>
<tr>
<td>Medium Risk</td>
<td>30 hours</td>
<td>9 days</td>
<td>45 days</td>
</tr>
<tr>
<td>High Risk</td>
<td>24 hours</td>
<td>3 days</td>
<td>45 days</td>
</tr>
</tbody>
</table>

USP Chapter 797
Chapter 797 Current Compliance

Based on report published by Critical Point, LLC:
• Overall 797 compliance 83%
• Hospital compliance in SC 67%
• Gowning compliance 83%
• Sterile glove use 92%
• Environmental sampling 81%
• Training and competency 78%

The USP Compliance Study by Critical Point Webinar sponsored by Pharmacy One Source
Hazardous Drug Compounding
Current Guidelines per 797

- Storage separate from non-hazardous drugs
- PECs-BSC or CACI
- CSTD use not mandatory
- SECs defined
- Low volume exception—two tier containment
- Gowning—chemo type gloves (no rating specified), no double gloving or double shoe covers
Current Regulatory Environment
Overview--Chapter 800

• Published February 1\textsuperscript{st}, 2016 in the First Supplement to USP 39

• USP Chapter 800 is to become official on December 1\textsuperscript{st} 2019

• Free USP 800 chapter download on the USP website
USP Chapter 800 Overview

• Addresses sterile AND non-sterile hazardous drug (HD) compounding
• Guidelines on practices and quality standards for handling of HDs to minimize personnel exposure
• Applies to all healthcare personnel including HD administration
• Very thoroughly addressing all aspects of hazardous drug manipulations
• Comprehensive approach to prevent worker as well as environmental exposure to HDs
USP Chapter 800 Overview

- List of hazardous drugs
- Types of exposure
- Responsibilities of personnel handling HDs
- Facilities and engineering controls
- Environmental quality and control
- PPE
- Hazard communication program
- Personnel training
- Receiving
USP Chapter 800 Overview

• Labeling, packaging, transport and disposal
• Dispensing final dosage forms
• Compounding
• Administering
• Deactivating, decontaminating, cleaning and disinfecting
• Spill control
• Documentation and SOPs
• Medical surveillance
USP Chapter 800 Overview

Requires HD list preparation

• List must be reviewed annually
• Based on NIOSH list
• Review exposure considerations
• Research drugs, MOAbs, CAR-T therapy?

https://virginiaintegrativepractice.com/mistletoe-cancer-therapy/
USP Chapter 800 Overview

PPE requirements

• Gowning key differences:
  – Double shoe covers
  – Hair cover
  – Mask
  – Solid front chemo gown
  – Double glove (ASTM 6978-05 chemo rated), the outer pair must be sterile

http://www.healthmark.ca
USP Chapter 800 Overview

Engineering Controls

• Primary engineering controls

• Secondary Engineering controls
  – ISO class 7
  – Containment segregated compounding area (C-SCA)

• Supplemental Engineering controls (CSTDs)
Class II Biological Safety Cabinet

Compounding Aseptic Containment Isolator

https://www.nuaire.com/products/pharmacy-isolators

Which one of these can be used to handle hazardous drugs?

- Compounding Aseptic Isolator
- Compounding Aseptic Containment Isolator

https://www.nuaire.com/products/pharmacy-isolators
**BUD Guidelines per USP 800**

<table>
<thead>
<tr>
<th>Use</th>
<th>PEC</th>
<th>SEC</th>
<th>Airflow</th>
<th>BUD</th>
</tr>
</thead>
<tbody>
<tr>
<td>To prepare sterile HDs in a cleanroom</td>
<td>BSC or CACI</td>
<td>ISO 7 negative air pressure</td>
<td>30 air exchanges, HEPA filtered air</td>
<td>As per 797</td>
</tr>
<tr>
<td>Compounding sterile HDs per 797</td>
<td>CACI</td>
<td>C-SCA, negative air pressure, unclassified</td>
<td>12 air exchanges per hour, exhaust</td>
<td>12 hours</td>
</tr>
<tr>
<td>Compounding low or medium risk HDs</td>
<td>BSC</td>
<td>C-SCA, negative air pressure, unclassified</td>
<td>12 air exchanges per hour, exhaust</td>
<td>12 hours</td>
</tr>
</tbody>
</table>
Supplemental Engineering Controls

- Closed System Transfer Devices (CSTDs)
- Not a substitute for PECs or SECs
- **Recommended** for use in compounding
- **Required** for administration
- NIOSH testing protocol for CSTDs currently proposed
USP Chapter 800 Overview

Medical Surveillance and Monitoring of Staff

• Controversial
• To establish comprehensive exposure control program
• Monitoring at baseline, then regularly, and exit exam
• Keep records of hours of HD handling exposure time, quantities, dosage forms
• Develop follow up plan for those that may have health changes suggesting toxicity exposure
USP 800 Current Readiness

• Start preparing NOW
• Familiarize yourself with guidelines
• Assign personnel responsibilities
• SOP development and updates
• Create hazardous drug list
• Evaluate engineering controls
Current Status of Chapter 797
Revision and Timeline

• Was proposed for public comment from 9/25/2015 to 1/31/2016

• Anticipated to be published for second round of public comments from 9/4/2018 to 11/30/2018

• Expected to be published 6/2/2019 and to become official 12/1/2019

• Current Chapter 797 from 6/1/2008 still official
Some of the Most Significant Suggested Chapter 797 Revisions

Proposed changes as of today….

• Expansion on guidelines for:
  – handling proprietary bag and vial systems
  – details on drug reconstitution according to the package insert (some BOPs don’t consider this compounding currently)
  – sterile injectable repackaging
Some of the Most Significant Suggested Chapter 797 Revisions

- Will require relative humidity limit (probably not more than 60%)
- Continuous monitoring of clean room conditions (temperature, pressure, humidity)
- Isolators (RABS)—no longer outside buffer area to get max BUD

https://www.setra.com/products#all
Some of the Most Significant Suggested Chapter 797 Revisions

• Most likely to change, as most controversial:
  – Going from 3 risk levels to 2 risk categories

• Beyond–use date changes
  • Category 1 (maximum BUD of 12 hours or less at RT, or 24 hours or less refrigerated)
  • Category 2 (BUD greater than 12 hours at RT, or greater than 24 hours refrigerated)

• BUD maximum of 45 days regardless of sterility testing

• “In-use time” specified
Some of the Most Significant Suggested Chapter 797 Revisions

• Removal of hazardous drug section
• Required monthly viable air and surface sampling
• Quarterly requirement for personnel monitoring
  – Visual observation of hand hygiene and gloving
  – Ongoing glove and fingertip sampling
Some of the Most Significant Suggested Chapter 797 Revisions

• Changes in gowning—requirement of not just sterile gloves but also STERILE SLEEVES and STERILE CLEANING TOOLS

• PPE and garb/glove requirements defined for each CSP category
Future Implications on Sterile Compounding

• Constantly changing and evolving environment
• Monitoring of FDA regulatory documents
• Sign up for the updates on USP website
• Evaluate your work practices, training, records
• Perform process gap analysis, update SOPs
• Evaluate current engineering controls
Future Implications on Sterile Compounding

• Change of the culture-keep seeking improvement
• Patient safety is always the #1 goal
Post Test Question 1

What is the role of USP in the pharmacy and medication management?

A. USP inspects pharmacies
B. USP provides guidelines and standards
C. USP regulates compounding
D. USP enforces its regulations
Post Test Question 2

USP Chapter 800 is already in effect.

TRUE

FALSE
Closed System Transfer Devices are required per USP 800 for handling of sterile hazardous medications when:

A. Unpacking
B. Compounding
C. Administering
D. Disposing
E. All of the above
Post Test Question 4

USP Chapter 800 requires all of the following engineering controls to be in place for Containment Segregated Area except:

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References

• USP Chapter 797 from USP 40, NF 35 official until May 1\textsuperscript{st}, 2018
• USP Chapter 800 from USP 40, NF 35 official until May 1\textsuperscript{st}, 2018
• Proposed USP Chapter 797 published September 25\textsuperscript{th} 2015
• The USP Compliance Study by Critical Point Webinar sponsored by Pharmacy One Source
• FDA.gov website
CE Evaluation Access Code

U81